REMARKS

I. The Subject Matter of the Claims

In general, the subject matter of the claims relates to antibodies that specifically bind protocadherin pc3.

II. The Objections to the Specification

Applicant noted four typographical errors in N-cadherin amino acids presented in Figure 1A-1C and corrected said errors in the response submitted May 7, 2004. Applicant submits that the corrections of the amino acids at positions 261 to threonine and at position 481 to tyrosine were clerical errors which have been corrected. The amino acids at positions 261 and 481 in Figures 1A-1C and SEQ ID NO: 98 correspond to amino acids 420 (Tyr) and 639 (Phe), respectively, of the N-cadherin sequence disclosed in Miyatani *et al.*, *Science*, 245:631-635 (1989).

These clerical errors have been corrected in the substitute drawings and sequence listing filed herewith. The sequences include no new matter since the N-cadherin sequence was available at the time of filing.

III. The Objection to the Drawings

The drawings have been amended to correct amino acids listed incorrectly and to clarify the beginning and end of the amino acid strings disclosed in the drawings. The amendments consist of addition of numbering at the end of each amino acid string to demarcate where in the protein sequence the amino acids are located. Additionally, the amino acid at position 116 in the figure was changed from threonine to serine, and the amino acid at position 150 was changed from valine to leucine. The drawings as amended are reflected in the Replacement Sheets, set out in Exhibit A. The changes to the drawings are reflected in the Annotated Sheets, set out in Exhibit B.

IV. Patentability Arguments

A. The Rejections of Claims 18, 21-22 Under 35 U.S.C. §101 May Properly Be Withdrawn

The Examiner maintains the rejection of claims 18 and 21-22 under 35 U.S.C. §101, asserting that the invention is not supported by a specific and substantial asserted or established utility.

MPEP 2107 (II) states that to provide evidence of utility, an applicant should explicitly identify a specific and substantial utility for the claimed invention and provide evidence that one of ordinary skill in the art would have recognized that the identified specific and substantial utility was well-established at the time of filing. MPEP 2107 also states that a rejection based on lack of utility should not be maintained if an asserted utility for the claimed invention would be considered specific, substantial, and credible by a person of ordinary skill in the art in view of all evidence of record. Further, a *prima facie* showing of lack of utility must establish that it is more likely than not that a person of ordinary skill in the art would not consider that any utility asserted by the applicant would be specific and substantial.

The claimed invention is *inter alia* directed to an antibody substance that binds to protocadherin pc3, and a hybridoma that secretes a monoclonal antibody specific for pc3. The specification sets out at page 7, lines 1-4, that antibodies of the invention are useful for purifying protocadherin pc3, identifying tissue or cellular expression of protocadherin pc3, and also as antagonists of binding activities of protocadherins, for example, cell-cell interactions. The specification also discloses, at page 2, lines 10-17, that the first cadherins described were identified by their unique immunological characteristics and tissue localization. For example, isolation of uvomorulin, one of the first cadherins identified, was carried out using anti-serum directed against an unknown surface protein (Vestweber *et al.*, *Exp. Cell Res.* 152:169-178, 1984, abstract submitted previously) and later localized to certain tissue sites using rabbit anti-serum (Boller *et al.*, *J. Cel Biol.* 100:327-32, 1985, submitted previously). These results indicate that even an antibody to an unknown cell-surface protein has substantial utility as recognized by one of ordinary skill.

It is well-established in the art that an antibody is useful in purifying a protein from its cellular environment and localizing a protein to a specific tissue or cellular fraction. The art is replete with examples of antibodies useful for purifying and isolating proteins of interest (See Vestweber *et al.*, *supra*; Boller *et al.*, *supra*), thereby providing a sound, objective basis for a substantial and credible utility for the antibodies of the invention. Further, recent disclosures in the art indicate that several protocadherin family members exhibit splice variants and other isoforms of the molecule (e.g., protocadherin-gamma, [Gayet et al., *FEBS Lett.* (2004) 578:175-9]; or, protocadherin-7 [Yoshida, *Cell Mol Biol Lett.* (2003) 8:735-41])(abstracts included in

Exhibit C). Antibodies to pc3 are useful in localizing and isolating pc3 splice variants and modulating activity of these variants.

It was also well-established at the time of filing that protocadherins mediate cell-cell aggregation, and that an antibody to a protocadherin (specifically pc43) is useful in isolating and modulating protocadherin activity. The Examiner cites to Suzuki(U), contending that Suzuki states that protocadherins are not involved in "typical cell-cell adhesion". Applicant emphasizes "typical cell-cell adhesion" and notes that Suzuki dos not rule out the role of protocadherins in cell-cell adhesion by the above statement. Indeed, Suzuki goes on to say that protocadherins may have a role in more general cell-cell interactions (page 2610, column 2nd full paragraph). Suzuki further states "If protocaherins play an important role as predicted, it should be exerted through the cytoplasmic domains and the cytoplasmic proteins," implying that protocadherin molecules play an important role in cell-cell interactions.

Moreover, the art describes numerous examples of a worker of ordinary skill in the art recognizing the utility of protocadherin molecules. A search of "protocadherin" in the National Library of Medicine Pubmed site returns over 100 search results (see exemplary pages included herewith). This search indicates that workers having ordinary skill in the art deem protocadherins an important family of molecules and further indicates that current studies of protocadherins point to significant biological activity for protocadherin molecules.

Recent studies have shown that protocadherins make up a family of over 50 molecules, and are involved in diverse biological activities [Suzuki, S. "Recent progress in protocadherin research", *Exp. Cell Res.* (2000) 261:13-8], such as cell-cell adhesion (Suzuki et al, *supra*), neural activities [Ahmed et al., "PCDH15 is expressed in the neurosensory epithelium of the eye and ear and mutant alleles are responsible for both USH1F and DFNB23" *Hum Mol Genet.* (2003) 12:3215-23], and actin activation [Moeller et al., "Protocadherin FAT1 binds Ena/VASP proteins and is necessary for actin dynamics and cell polarization". *EMBO J.* (2004) 23:3769-79] (abstracts included in Exhibit C). Protocadherins are recognized in the art as a valuable family of molecules involved in cell-cell adhesion and other biological functions. Moreover, comparison of protocadherin pc3 claimed herein and protocadherin sequences published subsequent to the priority date of the present application show that pc3 exhibits ~92% homology to human protocadherin beta 15 precursor (Genbank Accession No. NP_061758) (search results included in Exhibit C). Thus, the pc3 molecule described herein likely plays a

role in neural development similar to the role played by Pcdh 15 (Ahmed et al., *supra*) and other protocadherins.

Applicant submits that protocadherin pc3 polypeptide is patentable (see US 5,708,143) and, as such, an antibody binding to the molecule is also patentable. It is well-established in the art, and a person of ordinary skill would readily recognize, that an antibody to protocadherin pc3 possesses a specific, substantial and credible utility of modulating pc3 activity. It is not demonstrated by the examiner that it is more likely than not that a person of ordinary skill in the art would not consider that the utility asserted by the Applicant is specific and substantial. Therefore, the rejection of claims 18 and 21-22 under 35 U.S.C. § 101 should properly be withdrawn.

B. The Rejection of Claims 18, 21-22 Under 35 U.S.C. §112, First Paragraph, May Properly Be Withdrawn

The Examiner rejects claims 18 and 21-22 under 35 USC § 112, first paragraph, in conjunction with the 35 USC § 101 rejection. Applicant submits that the rejection under 35 USC § 101 has been overcome and, as such, the rejection under 35 USC § 112 may properly be withdrawn.

V. Conclusion

In view of the remarks made herein, Applicant submits that claims 18, 21-22 are in condition for allowance and respectfully request expedited notification of the same.

Respectfully submitted,

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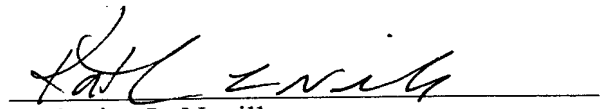
By: 

Katherine L. Neville
Reg. No: 53,379
Agent for Applicant

January 19, 2005

Amendment to the Drawings

Please replace the original drawings, Figure 1A-C, with substitute drawings Figure 1A-C, attached as Exhibit A. Annotated drawings marked to reflect the changes are submitted herewith in Exhibit B.

```
PC43   EC 1(29)ASTVIHYEIPEEREK-----GFAVGNVVANL--GLDLGSLSA-- (163)
       EC 2(136)PTQEMKLEISEAVAP-----GTRFPLESAH---DPDLGSNSL--(169)
       EC 3(245)NQSLYRARVPGGCTS-----GTRVVQVLAT---DLDEGPNGE-- (278)
       EC 4(355)TVTSVYSPVPEDAS------GTVIALLSVT---DLDAGENGL-- (385)
       EC 5(457)SQSSYDVYIEENNLP-----GAPILNLSVW---DPDAPQNAR-- (490)
       EC 6(569)LYPRPGGSSVEMLPRGTSA-GHLVSRVVGW---DADAGHNAW-- (604)

PC42   EC 1(42)VPEEQPPNTLI---------GSL----------AADYGFPDVG- (65)
       EC 2(147)ASPVITLAIPENTNI-----GSLFPIPLAS---DRDAGPNGV-- (180)
       EC 3(247)ERPSYEAELSENSPI-----GHSVIQVKAN---DSDQGANAE-- (280)
       EC 4(359)EIRGIGLVTHQDGMANISEDVAEETAVALVQVSDRDEGENAA-- (395)
       EC 5(473)TQSVTEVAFPENNKP-----GEVIAEITAS---DADSGSNAE-- (506)
       EC 6(578)MLSGYNFSVMENMPA-----LSPVGMVTVI---DGDKGENAQ-- (612)
       EC 7(682)TAPSNTSHKLLTPQTRL---GETVSQVAAE---DFDSGVNAE-- (717)

FAT    EC18(1) EDTVYSFDIPENAQR-----GYQVGQIVAR---DADLGQNAQ-- (34)

N-CAD  EC 1(1)DWVIPPINLPENSRG-----PFPQELVRIRS--DRDKNLSLRYT (37)
       EC 2(104)LHQVWNGTVPEGSKP-----GTYVMTVTAI---DADDPNALNGM (144)
       EC 3(224)TAMTFYGEVPENRVD-----IIVANLTVT----DKDQPHTPAWN (258)
       EC 4(334)APNPKIIRQEEGLHA-----GTMLTTFTAG---DPDRYMQQN-- (372)
       EC 5(443)LPQEAETCETPDPNSINITTAL----------DYDIDPNAGP- (478)

MOTIF        ****o***v*En*****-----Gt*v**v*A*---D*D*G*N**--
```

FIGURE 1A

Annotated Sheet

FIGURE 1B

Annotated Sheet

```
PC43   EC 1(92)LDRLELCGTLPSCTVTLELVVENP----------LELFSVEVVIQDINDNNPAF (135)
       EC 2(203)LDREREPSLQLVLTALDGGTPAL----------SASLPIHIKVLDANDNAPVF (244)
       EC 3(310)LDFEDTKLHEIYIQAKDKGANPE----------GAHCKVLVEVVDVNDNAPEI (352)
       EC 4(414)LDRETVPEYNLSITARDAGTPSL----------SALTIVRVQVSDINDNPPQS (456)
       EC 5(524)LDYEDRREFELTAHISDGGTPVL----------ATNISVNIFVTDRNDNAPQV (566)
       EC 6(694)QDTDSPRQTLTVL-IKDNGEPSLSTTATLTVSVTEDSPEARAEFPSGSAPREQKKN (698)

PC42   EC 1(93)IDREGLRECQNQLPGDPCILEFEVSITDLVQNAS--PRLLEGQIEVQDINDNTPNF (146)
       EC 2(204)LDRERWDSYDLTIKVQDGGSPPR----------ATSALLRVTVLDTNDNAPKF (246)
       EC 3(311)VDREDLSTLRFSVLAKDRGTNPK----------SARAQVVVTVKDMNDNAPTI (353)
       EC 4(430)LDYEKVKDYTIEIVAVDSGNPPL----------SSTNSLKVQVVDVNDNAPVF (472)
       EC 5(534)LDREQRESYELKVVAADRGSPSL----------QGTATVLVNVLDCNDNDPKF (578)
       EC 6(639)FDREQQSTYTFQLKAVDGGVPPR----------SAYVGVTINVLDENDNAPYI (681)
       EC 7(746)IERRHHGLHRLVVKVSDRGKPPRYGTALVHLYVNETLANRTLLETLLGHSLDTPLD (801)
                                                  IDIAGDPEYERSKQRGN (818)

FAT    EC18(63)LDYEEVQHYILIVQAQDNGQPSL----------STTITVYCNVLDLNDNAPIF (105)

N-CAD  EC 1(66)LDREQIARFHLRAHAVDINGNQV----------ENPIDIVINVIDMNDNRPEF (108)
       EC 2(178)LDRENVQQYTLIIQATDMEGIPTYGL----------SNTATAVITVTDVNDNPPEF (223)
       EC 3(291)IDFETNRMFVLTVAAENQVPLAKGIQHPP-------QSTATVSVTVIDVNE-NPYF (338)
       EC 4(400)LDRESPNVKNNIYNATFLASDNGIPPM---------SGTGTLQIYLLDINDNAPQV (446)
       EC 5(510)IKFLEAGIYEVPIIITDSGNPPKSNIS---------ILRVRVCQCDFNGDCTDVDR (557)

MOTIF        LDRE****o*L*v*A*D*G*P**----------**T*Tv*v*V*D*NDNAP*F
```

FIGURE 1C

Annotated Sheet

1: FEBS Lett. 2004 Dec 3;578(1-2):175-9.

The b1 isoform of protocadherin-gamma (Pcdhgamma) interacts with the microtubule-destabilizing protein SCG10.

Gayet O, Labella V, Henderson CE, Kallenbach S.

Institut de Biologie du Developpement de Marseille, Marseille, France.

Due to their structural characteristics and their diversity, the 22 members of the protocadherin-gamma (Pcdhgamma) family have been suggested to contribute to the establishment of specific connections in the nervous system. Here, we focus on a single isoform, Pcdhgamma-b1. Its expression is found in different brain regions and in developing spinal cord it is restricted to scattered cells, whereas all cells are labeled using an antibody that recognizes all Pcdhgamma isoforms. As a first step to understanding the signaling mechanisms downstream of Pcdhgamma, we identify the microtubule-destabilizing protein SCG10 as a cytoplasmic interactor for Pcdhgamma-b1 and other isoforms of the Pcdhgamma-b subfamily, and show that SCG10 and Pcdhgamma-b1 are found together in certain neuronal growth cones.

PMID: 15581637 [PubMed - in process]

1: Cell Mol Biol Lett. 2003;8(3):735-41.

Fibroblast cell shape and adhesion in vitro is altered by overexpression of the 7a and 7b isoforms of protocadherin 7, but not the 7c isoform.

Yoshida K.

Genetic Diagnosis, Institute of Medical Science, University of Tokyo, 4-6-1 Shirokanedai, Minato-ku, Tokyo 108-8639, Japan. yoshidak@ims.u-tokyo.ac.jp

Protocadherins (Pcdhs) are a family of cadherins considered to play an important role in the cell-cell adhesion of specific neurons in the central nervous system. Of the reported Pcdhs, relatively little is known about the functional role of protocadherin 7 (Pcdh7), and there is no evidence of Pcdh7 mediated cell-cell adhesion. To date, three splicing variants are known; they may have different effects on cell phenotype. We report here that mouse fibroblast L cells stably overexpressing the Pcdh7 isoforms 7a and 7b, but not 7c, showed a morphological change and Ca(2+)dependent cell adhesion.

PMID: 12949613 [PubMed - indexed for MEDLINE]

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Alternatively spliced variants of protocadherin 8 exhibit distinct patterns of expression during mouse development.
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PMID: 15627506 [PubMed - in process]

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Hum Mol Genet. 2004 Dec 8; [Epub ahead of print]
PMID: 15590703 [PubMed - as supplied by publisher]

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The b1 isoform of protocadherin-gamma (Pcdhgamma) interacts with the microtubule-destabilizing protein SCG10.
FEBS Lett. 2004 Dec 3;578(1-2):175-9.
PMID: 15581637 [PubMed - in process]

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EMBO J. 2004 Sep 29;23(19):3769-79. Epub 2004 Sep 02.
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1: Exp Cell Res. 2000 Nov 25;261(1):13-8.

Recent progress in protocadherin research.

Suzuki ST.

Division of Developmental Biology, Institute for Developmental Research, Aichi Human Service Center, 713-8 Kamiya-cho, Kasugai-shi, Aichi, 480-0392, Japan. stsuzuki@cc.nagoya-u.ac.jp

Protocadherins constitute a large family belonging to the cadherin superfamily and function in different tissues of a wide variety of multicellular organisms. Protocadherins have unique features that are not found in classic cadherins. Expression of protocadherins is spatiotemporally regulated and they are localized at synapses in the CNS. Although protocadherins have Ca(2+)-dependent homophilic interaction activity, the activities are relatively weak. Some protocadherins have heterophilic interaction activity and the cytoplasmic domains associate with the unique cytoplasmic proteins, which are essential for their biological functions. Given the characteristic properties, the large size, and the diversity of members of the protocadherin family, protocadherins may participate in various biological processes. In particular, protocadherins seem to play a central role(s) in the CNS as related to synaptic function. Copyright 2000 Academic Press.

Publication Types:
- Review
- Review, Tutorial

PMID: 11082270 [PubMed - indexed for MEDLINE]

1: Hum Mol Genet. 2003 Dec 15;12(24):3215-23. Epub 2003 Oct 21.

PCDH15 is expressed in the neurosensory epithelium of the eye and ear and mutant alleles are responsible for both USH1F and DFNB23.

Ahmed ZM, Riazuddin S, Ahmad J, Bernstein SL, Guo Y, Sabar MF, Sieving P, Riazuddin S, Griffith AJ, Friedman TB, Belyantseva IA, Wilcox ER.

Section of Human Genetics, Laboratory of Molecular Genetics, National Institute on Deafness and Other Communication Disorders, National Institutes of Health, Rockville, MD, USA.

Recessive splice site and nonsense mutations of PCDH15, encoding protocadherin 15, are known to cause deafness and retinitis pigmentosa in Usher syndrome type 1F (USH1F). Here we report that non-syndromic recessive hearing loss (DFNB23) is caused by missense mutations of PCDH15. This suggests a genotype-phenotype correlation in which hypomorphic alleles cause non-syndromic hearing loss, while more severe mutations of this gene result in USH1F. We localized protocadherin 15 to inner ear hair cell stereocilia, and to retinal photoreceptors by immunocytochemistry. Our results further strengthen the importance of protocadherin 15 in the morphogenesis and cohesion of stereocilia bundles and retinal photoreceptor cell maintenance or function.

PMID: 14570705 [PubMed - indexed for MEDLINE]

1: EMBO J. 2004 Sep 29;23(19):3769-79. Epub 2004 Sep 02.

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Protocadherin FAT1 binds Ena/VASP proteins and is necessary for actin dynamics and cell polarization.

Moeller MJ, Soofi A, Braun GS, Li X, Watzl C, Kriz W, Holzman LB.

[1] Institute for Anatomy and Cell Biology, University of Heidelberg, Heidelberg, Germany [2] Department of Internal Medicine, University of Michigan Medical School, Ann Arbor, MI, USA.

Cell migration requires integration of cellular processes resulting in cell polarization and actin dynamics. Previous work using tools of Drosophila genetics suggested that protocadherin fat serves in a pathway necessary for determining cell polarity in the plane of a tissue. Here we identify mammalian FAT1 as a proximal element of a signaling pathway that determines both cellular polarity in the plane of the monolayer and directed actin-dependent cell motility. FAT1 is localized to the leading edge of lamellipodia, filopodia, and microspike tips where FAT1 directly interacts with Ena/VASP proteins that regulate the actin polymerization complex. When targeted to mitochondrial outer leaflets, FAT1 cytoplasmic domain recruits components of the actin polymerization machinery sufficient to induce ectopic actin polymerization. In an epithelial cell wound model, FAT1 knockdown decreased recruitment of endogenous VASP to the leading edge and resulted in impairment of lamellipodial dynamics, failure of polarization, and an attenuation of cell migration. FAT1 may play an integrative role regulating cell migration by participating in Ena/VASP-dependent regulation of cytoskeletal dynamics at the leading edge and by transducing an Ena/VASP-independent polarity cue.

PMID: 15343270 [PubMed - in process]

Blast 2 Sequences results

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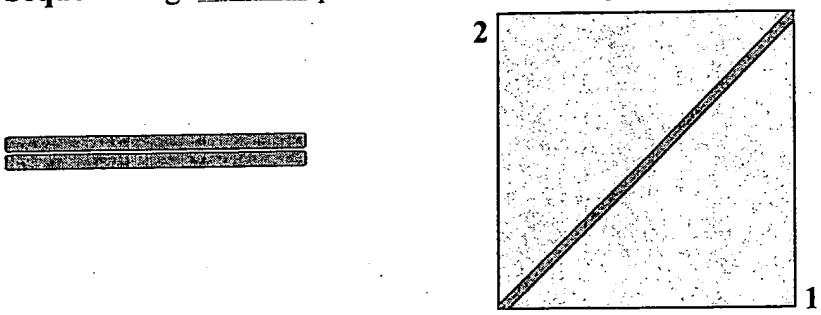
BLAST 2 SEQUENCES RESULTS VERSION BLASTP 2.2.10 [Oct-19-2004]

Matrix BLOSUM62 gap open: 11 gap extension: 1
x_dropoff: 50 expect: 10.000 wordsize: 3 Filter Align

Sequence 1 lcl|seq_1 **Length** 787 (1 .. 787)

Sequence 2 gi 9256610 protocadherin beta 15 precursor [Homo sapiens] **Length** 787 (1 .. 787)



NOTE:The statistics (bitscore and expect value) is calculated based on the size of nr database

```
Score = 1418 bits (3670), Expect = 0.0
Identities = 727/787 (92%), Positives = 728/787 (92%)
```

```
Query:                   1   MEPAGERFPEQRQVXXXXXXXEVTLAGWEPRRYSVMEETERGSFVANLANDLGLGVGELA 60
                             MEPAGERFPEQRQV       EVTLAGWEPRRYSVMEETERGSFVANLANDLGLGVGELA
Sbjct:                   1   MEPAGERFPEQRQVLILLLLLEVTLAGWEPRRYSVMEETERGSFVANLANDLGLGVGELA 60
protocadherin beta 15 27                          **********************************
sig_peptide              1   **************************

Query:                  61   ERGARVVSEDNEXXXXXXXXXXXXXNEKLDREKLCGPTEPCIMHFQVLLKKPLEVFRAE 120
                             ERGARVVSEDNE              NEKLDREKLCGPTEPCIMHFQVLLKKPLEVFRAE
Sbjct:                  61   ERGARVVSEDNEQGLQLDLQTGQLILNEKLDREKLCGPTEPCIMHFQVLLKKPLEVFRAE 120
protocadherin beta 15 61   ************************************************************

Query:                 121   LLVTDINDHSPEFPEREMTLKIPETSSLGTVFPLKKARDLDVGSNNVQNYNISPNSHFHV 180
                             LLVTDINDHSPEFPEREMTLKIPETSSLGTVFPLKKARDLDVGSNNVQNYNISPNSHFHV
Sbjct:                 121   LLVTDINDHSPEFPEREMTLKIPETSSLGTVFPLKKARDLDVGSNNVQNYNISPNSHFHV 180
protocadherin beta 15 121  ************************************************************

Query:                 181   STRTRGDGRKYPELVLDTELDREEQAELRLTLTAVDGGSPPRSGTVQILILVLDANDNAP 240
                             STRTRGDGRKYPELVLDTELDREEQAELRLTLTAVDGGSPPRSGTVQILILVLDANDNAP
Sbjct:                 181   STRTRGDGRKYPELVLDTELDREEQAELRLTLTAVDGGSPPRSGTVQILILVLDANDNAP 240
protocadherin beta 15 181  ************************************************************

Query:                 241   EFVQALYEVQVPENSPVGSLVVKVSARDLDTGTNGEISYSLYYSSQEIDKPFELSSLSGE 300
                             EFVQALYEVQVPENSPVGSLVVKVSARDLDTGTNGEISYSLYYSSQEIDKPFELSSLSGE
Sbjct:                 241   EFVQALYEVQVPENSPVGSLVVKVSARDLDTGTNGEISYSLYYSSQEIDKPFELSSLSGE 300
protocadherin beta 15 241  ************************************************************
```

```
Query:                  301 IRLIKKLDFETMSSYDLDIEASDGGGLSGKCSVSVKVLDVNDNFPELSISSLTSPIPENS 360
                            IRLIKKLDFETMSSYDLDIEASDGGGLSGKCSVSVKVLDVNDNFPELSISSLTSPIPENS
Sbjct:                  301 IRLIKKLDFETMSSYDLDIEASDGGGLSGKCSVSVKVLDVNDNFPELSISSLTSPIPENS 360
protocadherin beta 15 301 ************************************************************

Query:                  361 PETEVALFRIRDRDSGENGKMICSIQDDVPFKLKPSVENFYRLVTEGALDRETRAEYNIT 420
                            PETEVALFRIRDRDSGENGKMICSIQDDVPFKLKPSVENFYRLVTEGALDRETRAEYNIT
Sbjct:                  361 PETEVALFRIRDRDSGENGKMICSIQDDVPFKLKPSVENFYRLVTEGALDRETRAEYNIT 420
protocadherin beta 15 361 ************************************************************

Query:                  421 ITITDLGTPRLKTEQSITVLVSDVNDNAPAFTQTSYTLFVRENNSPALHIGSVSATDRDS 480
                            ITITDLGTPRLKTEQSITVLVSDVNDNAPAFTQTSYTLFVRENNSPALHIGSVSATDRDS
Sbjct:                  421 ITITDLGTPRLKTEQSITVLVSDVNDNAPAFTQTSYTLFVRENNSPALHIGSVSATDRDS 480
protocadherin beta 15 421 ************************************************************

Query:                  481 GTNAQVTYSLLPPQDPHLPLTSLVSINTDNGHLFALQSLDYEALQAFEFRVGATDRGFPA 540
                            GTNAQVTYSLLPP+DPHLPLTSLVSINTDNGHLFALQSLDYEALQAFEFRVGATDRGFPA
Sbjct:                  481 GTNAQVTYSLLPPRDPHLPLTSLVSINTDNGHLFALQSLDYEALQAFEFRVGATDRGFPA 540
protocadherin beta 15 481 ************************************************************

Query:                  541 LSSEALVRVLVLDANDNSPFVLYPLQNGSAPCTELVPRAAEPGYLVTKVVAVDGDSGQNA 600
                            LSSEALVRVLVLDANDNSPFVLYPLQNGSAPCTELVPRAAEPGYLVTKVVAVDGDSGQNA
Sbjct:                  541 LSSEALVRVLVLDANDNSPFVLYPLQNGSAPCTELVPRAAEPGYLVTKVVAVDGDSGQNA 600
protocadherin beta 15 541 ************************************************************

Query:                  601 WLSYQLLKATEPGLFGVWAHNGEVRTARLLSERDVAKHRLVVLVKDNGEPPRSATATLQV 660
                            WLSYQLLKATEPGLFGVWAHNGEVRTARLLSERDVAKHRLVVLVKDNGEPPRSATATLQV
Sbjct:                  601 WLSYQLLKATEPGLFGVWAHNGEVRTARLLSERDVAKHRLVVLVKDNGEPPRSATATLQV 660
protocadherin beta 15 601 ************************************************************

Query:                  661 LLVDGFSXXXXXXXXXXXXXXXXDSLTVYXXXXXXXXXXXXXXXXXXXXXXRLCRRSRAA 720
                            LLVDGFS                DSLTVY                     RLCRRSRAA
Sbjct:                  661 LLVDGFSQPYLPLPEAAPAQAQADSLTVYLVVALASVSSLFLFSVFLFVAVRLCRRSRAA 720
protocadherin beta 15 661 ************************************************************

Query:                  721 SVGRCSVPEGPFPGHLVDVSGTGTLSQSYQYEVCLTGGSESNDFKFLKPIFPNIVSQDSR 780
                            SVGRCSVPEGPFPGHLVDVSGTGTLSQSYQYEVCLTGGSESNDFKFLKPIFPNIVSQDSR
Sbjct:                  721 SVGRCSVPEGPFPGHLVDVSGTGTLSQSYQYEVCLTGGSESNDFKFLKPIFPNIVSQDSR 780
protocadherin beta 15 721 ************************************************************

Query:                  781 RKSEFLE 787
                            RKSEFLE
Sbjct:                  781 RKSEFLE 787
protocadherin beta 15 781 *******

CPU time:     0.06 user secs.      0.01 sys. secs.        0.07 total secs.

Lambda      K       H
   0.314    0.133    0.379

Gapped
Lambda      K       H
   0.267   0.0410    0.140

Matrix: BLOSUM62
Gap Penalties: Existence: 11, Extension: 1
Number of Sequences: 1
Number of Hits to DB: 5083
Number of extensions: 2666
```

```
Number of successful extensions: 33
Number of sequences better than 10.0: 1
Number of HSP's better than 10.0 without gapping: 1
Number of HSP's gapped: 1
Number of HSP's successfully gapped: 1
Number of extra gapped extensions for HSPs above 10.0: 0
Length of query: 787
Length of database: 784,226,776
Length adjustment: 139
Effective length of query: 648
Effective length of database: 784,226,637
Effective search space: 508178860776
Effective search space used: 508178860776
Neighboring words threshold: 9
Window for multiple hits: 0
X1: 16 ( 7.3 bits)
X2: 129 (49.7 bits)
X3: 129 (49.7 bits)
S1: 42 (21.9 bits)
S2: 81 (35.8 bits)
```